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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/760,590	01/16/2001	Kurt M. Kesseler	HMR 2041 US NPI	4289

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AVENTIS PHARMACEUTICALS, INC.  
PATENTS DEPARTMENT  
ROUTE 202-206, P.O. BOX 6800  
BRIDGEWATER, NJ 08807-0800

[REDACTED] EXAMINER

CHANG, CELIA C

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 02/01/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	09/760,590	KESSELER, KURT M.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Celia Chang	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY-PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 15 June 2001.
- 2a) This action is **FINAL**.      2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-9 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 1-9 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

- 13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) The translation of the foreign language provisional application has been received.
- 15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

- |  |  |
|--|--|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.<br>6) <input type="checkbox"/> Other: |  |

### **DETAILED ACTION**

1. Claims 1-9 are in the case.
2. Claims 1, 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicants' attention is drawn to that chemical "product" are identified with the molecular formula i.e. elemental content, bonding arrangement, stereo/optical orientation etc. and physical characteristics i.e. crystal, amorphous, oil etc. Merit for patentability is considered on the chemical and physical character of the "product". It is unclear what is the claimed subject matter is it a new form of an old product or is it a new product with distinct molecular formula and physical character. Please note that in the reference Kattige et al. US 4,900,727 each product is identified by the structure formula, content of other ingredients i.e. addition salt or hydrating water with distinct melting points (see col. 6 table 4 lines 12-13). Ordinary skilled person in the art would recognize that a product differ in elemental content and melting point are independent and distinct products.

The instant claims being drawn to "form II" of (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxyl-8[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one is ambiguous and confusing while the specification defines form II is a "solvate of ethanol" with (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxyl-8[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one is conflicting and indefinite.

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-4, 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kattige et al. US 4,900,727 and Sedlacek et al. (both cited on 1449) in the event that the claims are drawn

to new form of old product of (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxyl-8[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one.

Determination of the scope and content of the prior art (MPEP §2141.01)

Kattige et al. US 4,900,727 and Sedlacek et al. disclosed solid form of (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxy-8[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one, see '727 col. 22, claim 4, or Sedlacek p.1146-1147 flavopiridol and its pharmacological efficacy in treating cancer, inhibiting protein kinase or cyclin dependent kinase (see p.1146-1164).

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Kattige et al. US 4,900,727 and Sedlacek et al. disclosed all the elements of the claims except the physical nature of the solid material was not described.

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One would find the instant claims being drawn to the particular crystalline form I prima facie obvious over the art because changing the form, purity or other characteristic of an old product does not render the novel form patentable when the change is a mere difference in degree of purity or physical character of the “product” for which the chemical nature and therapeutic activity were the same. See In re Cofer 148 USPQ 268, Ex parte Schmidt-Kastner 153 USPQ 473.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kim US 5,908,934 in view of Cheronis and Evans in the event the claims are drawn to an ethanol solvate of (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxyl-8[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one.

Determination of the scope and content of the prior art (MPEP §2141.01)

Kim '934 disclosed methanol solvate of (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxyl-8[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one and analogous process in preparing the solvate, see col. 9 lines 50-57.

Ascertainment of the difference between the prior art and the claims (MPEP §2141.02)

Kim '934 disclosed all the elements of the claims except the solvent employed by Kim '934 is methanol and during the crystallization stage a paired solvent of methanol/ether was used, while the instant claims are drawn to the homologous ethanol.

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Cheronis taught that choice of solvent in crystallization is empirical and one should experimentally select under the general guidelines (see p.32 section 5.3). When solubility of the compound in a particular solvent is too high, solvent pair may be employed (see p.35).

Finding of prima facie obviousness—rational and motivation (MPEP§2142-2143)

One having ordinary skill in the art would find the claimed product and process prima facie obvious over Kim because :

- (i) person having ordinary skill in the art is deemed to be aware of that the (-)-cis-2-(2-chlorophenyl)-5,7-dihydroxyl-8[4R-(3S-hydroxy-1-methyl)piperidinyl]-4H-1-benzopyran-4-one solvate is an organic clathrate. The nature of organic clathrate is that the guest molecules are mechanically imprisoned in the framework of the host (see Fox p.394 paragraph below fig). Therefore, the next homolog of methanol, i.e. the ethanol would be a close analog for such clathrate formation.
- (ii) person having ordinary laboratory skill in synthetic chemistry in possession of the exemplified process and product of methanol solvent by Kim and the laboratory manual of Cheronis would be motivate to empirically modify the process with the next homologous alcohol with the expectation that ethanol solvate with a different solubility can be obtained without pairing solvents.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celia Chang whose telephone number is 703-308-4702. The examiner can normally be reached on Monday through Thursday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner can be reached by facsimile at (703) 308-7922 with courtesy voice message supra.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.



Celia Chang  
Primary Examiner  
Art Unit 1625

CCPC/Chang

Jan. 31, 2001